



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/280,567 | 03/30/1999 | THOMAS FRANK BUMOL | 0409020136 | 5988 |

25885 7590 07/12/2004

ELI LILLY AND COMPANY
PATENT DIVISION
P.O. BOX 6288
INDIANAPOLIS, IN 46206-6288

EXAMINER

BRANNOCK, MICHAEL T

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1646

DATE MAILED: 07/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------------|-------------------------------------|--|
| Office Action Summary | Application No. 09/280,567 | Applicant(s) BUMOL ET AL. | |
| | Examiner Michael Brannock | Art Unit 1646 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 April 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4,5,7-35 and 40-43 is/are pending in the application.
- 4a) Of the above claim(s) 4,5 and 7-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 40-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application: Claims and Amendments

Previously pending claims 1-3, 6, 36-39 are canceled. Non elected claims 4, 5, 7-35 have been withdrawn from consideration, as set forth previously. Claims 40-43 are under examination.

Response to Arguments

Applicant is notified that any outstanding rejection or objection that is not expressly maintained in this Office action has been withdrawn in view of Applicant's amendments.

Maintained Rejection:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 40-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent Application Publication 2002/0065210, which claims priority to provisional application 60/094,640 filed July 30, 1998, in view of Nagata et al. Science, 267(1449-1456)1995, as set forth previously and reiterated below.

The instantly claimed methods derive from the discovery that FLINT proteins (e.g. SEQ ID NO: 6 and 8) can disrupt the FasL-Fas receptor interaction, see page 6, L26-30 of the instant specification for example. The FasL-Fas receptor interaction is well established in the art as

Art Unit: 1646

being a key mediator of apoptosis in a variety of cell types, see the Abstract of Nagata et al., and particularly of apoptosis of liver cells in hepatitis, see the second full paragraph of col 3 of page 1454 of Nagata et al. US Patent Application Publication 2002/0065210 discloses that a protein that they term “Decoy Receptor 3” or “DcR3”, and is 100% identical to the mature form of SEQ ID NO: 6, that can inhibit FasL-Fas receptor induced apoptosis, see page 5, paragraph 0064. This teaching is also found in the 60/094,640 application at page 23. The 2002/0065210 publication teaches that DcR3 can be employed therapeutically to regulate apoptosis by Fas ligand, e.g. as an antagonist to inhibit Fas induced apoptosis (paragraphs 0124 and 0126, see also page 23 of 60/094,640).

However, the 2002/0065210 publication does not specifically mention the Fas-mediated apoptosis that occurs in the liver during the pathogenesis of the disorders recited in the instantly claimed methods. However, this Fas-mediated involvement in the liver was well established in the art at the time the 60/099,643 application was filed, as exemplified by Nagata et al., discussed above. Thus, it would be obvious to one of ordinary skill in the art, at the time the invention was made, and with reasonable expectation of success, to therapeutically employ a polypeptide having an amino acid sequence 100% identical to SEQ ID NO: 6 so as to inhibit Fas-mediated apoptosis, as taught by the 2002/0065210 publication, and to do so to treat individuals suffering from disorders of the liver, required by the claims, wherein apoptosis was well established to underlie such disorders, and in particular Fas-mediated apoptosis as taught by Nagata et al. The motivation to do so is provided by the 2002/0065210 publication wherein it is taught that DcR3 is believed to be a decoy receptor that inhibits Fas-mediated apoptosis (e.g.

page 6, L26-30) and by Nagata who teach that Fas mediates apoptosis of hepatocytes during hepatitis (see page 1454, col 3, second full paragraph).

Applicant argues that the SEQ ID NO: 6 represents that mature form of the polypeptide, i.e., lacking the signal sequence positions 1-29 of the full length protein which is neither taught or suggested by the publication. This argument has been fully considered but not deemed persuasive. The instant claims are not limited to a polypeptide consisting of SEQ ID NO: 6 or 8. The claims recite a polypeptide having the sequence of SEQ ID NO: 6; the full length polypeptide *has* the sequence of SEQ ID NO: 6. The word "having" is considered to be open language, equivalent in this case to the word "comprising".

It should be noted that one of ordinary skill in the art would appreciate from Fig 6 of the 2002/0065210 publication that the small arrow between residues 23 and 24 indicates the putative cleave point of the signal peptide. This is born-out by Pitti-RM et al., Nature 396(699-703)1998 wherein the same figure is presented and the arrow is indicated to represent the cleavage point, see Figure 1a. This cleavage point is different than that of the instant application which occurs between positions 29-and 30. Several subsequent reports support Applicant's determination of the cleavage point, see the first paragraph of col 2 of page 13734 of Kang-Yeol-Y et al., J. Biol. Chem. 274(20)13733-6, 1999 and col 2 of page 1231 of Bai-C. et al., PNAS 97(3)1230-1235, 2000. Never-the-less, the instant claims are not so limited, as discussed above.

Conclusion:

This application contains claims 4, 5, 7-35 drawn to an invention nonelected with traverse in Applicant's response of April 3, 2000. A complete reply to the final rejection must include

Application/Control Number: 09/280,567

Page 5

Art Unit: 1646

cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP

§ 821.01.

ly
7/5/04

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

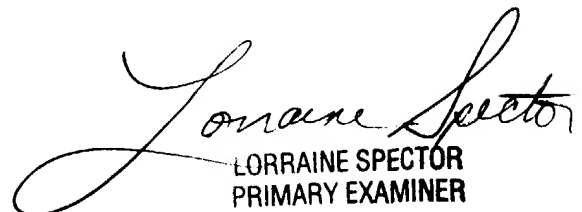
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, Ph.D., can be reached at (571) 272-0961.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

July 8, 2004


LORRAINE SPECTOR
PRIMARY EXAMINER